COLLEGE OF ENGINEERING / DEPARTMENT OF MATERIALS SCIENCE AND ENGINEERING

Oxygen-Sensitive Electrosprayed Core-Shell Polymer Microparticles for Biological Applications

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INTRODUCTION

The development of luminescent oxygen-sensitive core-shell polymer microparticles can provide beneficial advantages to biological applications. The objective of this research is to create optimal oxygen sensitive microparticles in an injectable form to detect hypoxic regions within tissue indicative of areas of low oxygen concentration associated with tumor recurrence that often resists traditional cancer treatments.

BACKGROUND

Since oxygen quenches a phosphorescent output from oxygen-sensitive molecules, decreases in oxygen concentration in biological tissue can be observed by an increased phosphorescent output. [1]

- Hypoxic regions correlated with the development of small tumors in tissue

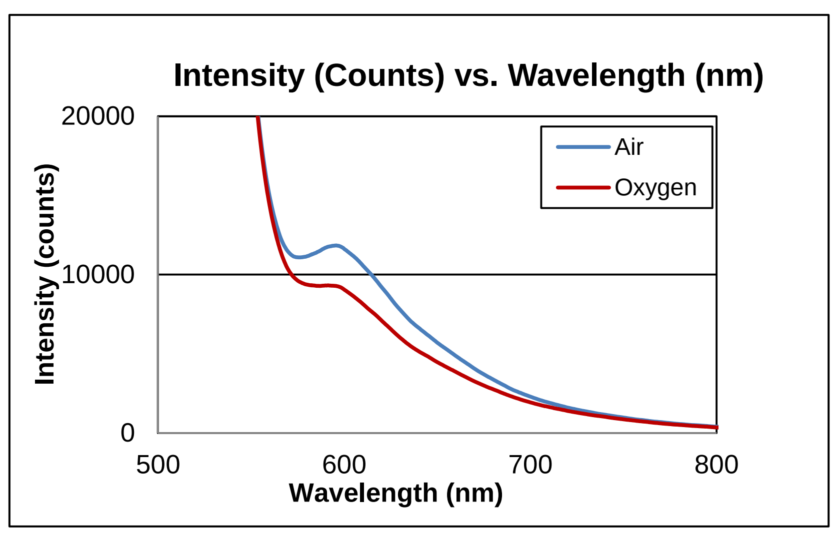


Figure 1: Representation of oxygen quenching the phosphorescent output from the oxygen-sensitive molecules

Previous research in the lab has incorporated these molecules into electrospun scaffolds leading to better response characteristics. [2]

- **Desired:** Extend to biological applications where tissue penetration is a limiting factor

Luminescent oxygen sensors typically require violet or blue excitation, which does not penetrate tissue deeply because of high levels of absorption and scattering through the tissue layers. [3]

- **Solution:** Develop upconverting nanoparticles (UCNPs) in combination with the oxygen-sensitive molecule, $Ru(dpp)_3Cl_2$ as injectable electrosprayed particles
- Near Infrared (NIR) penetrates tissue more easily
- UCNPs can emit blue light upon NIR excitation which locally triggers an oxygen-sensitive molecule ("Handshake" Interaction)

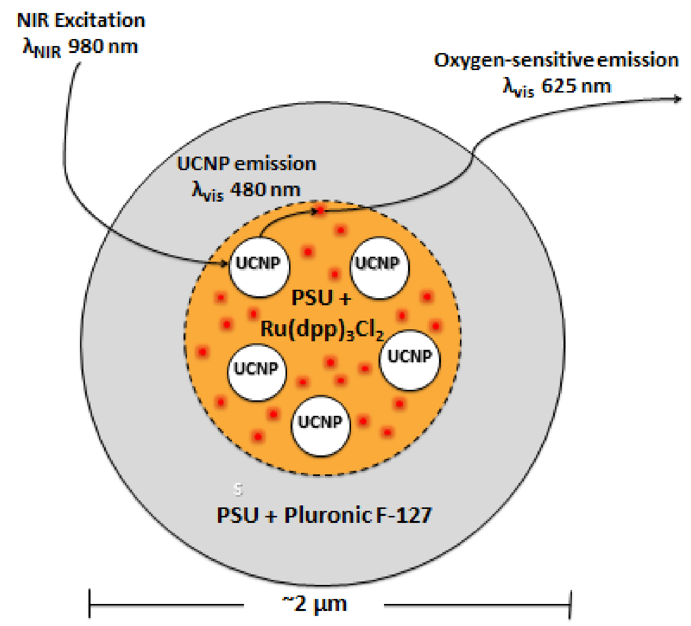


Figure 2: "Handshake "Interaction between UCNPs and Oxygen-Sensitive Dye

AIM

To develop these optimal injectable microparticles, the current research objectives are:

1) Proper microparticle core-shell morphology
2) Dispersion of microparticles within solution
3) Analyzation of particle leaching behavior

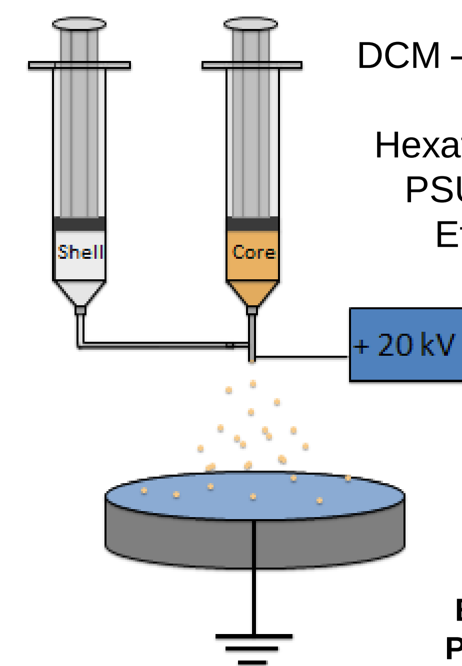
METHODS

Electrospraying - a technique of converting polymer solution into fine droplets by administering electrical forces.

Solution

Core (flow rate: 0.1-0.5 mL/hr): 1wt% PSU in 75/25 DCM/HFP + 0.5 wt% oxygen sensing dye + 8 wt% UCNPs

Shell (flow rate: 0.5-1.5 mL/hr): 1 wt% PSU in 75/25 DCM/HFP mixture + 1 wt% Pluronic F-127



DCM – Dichloromethane
HFP - Hexafluoroisopropanol
PSU – Polysulfone
EtOH - Ethanol

Figure 3: Electrospraying Process Diagram

MORPHOLOGY RESULTS

- Analyzed samples with SEM (Scanning Electron Microscopy)
  - Varied electrospraying parameters and solutions
  - Specific qualities analyzed
    - Porosity, diameter size, possible fiber formation
- ***Optimal Parameters:***
- *Solvent Ratio: 75/25 DCM/HFP*
- *Polymer: 1 wt%*
- *Flow Rate: shell/core: 0.3/0.5 mL/hr*
- *Distance: 20 cm*

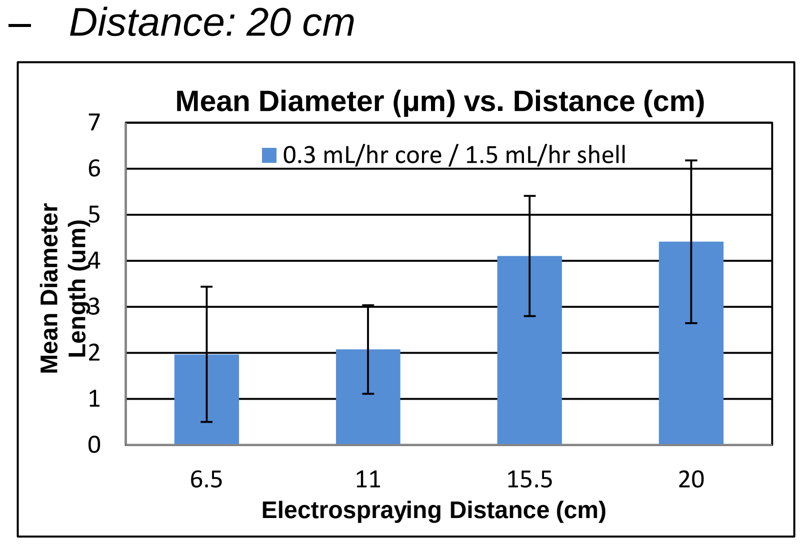
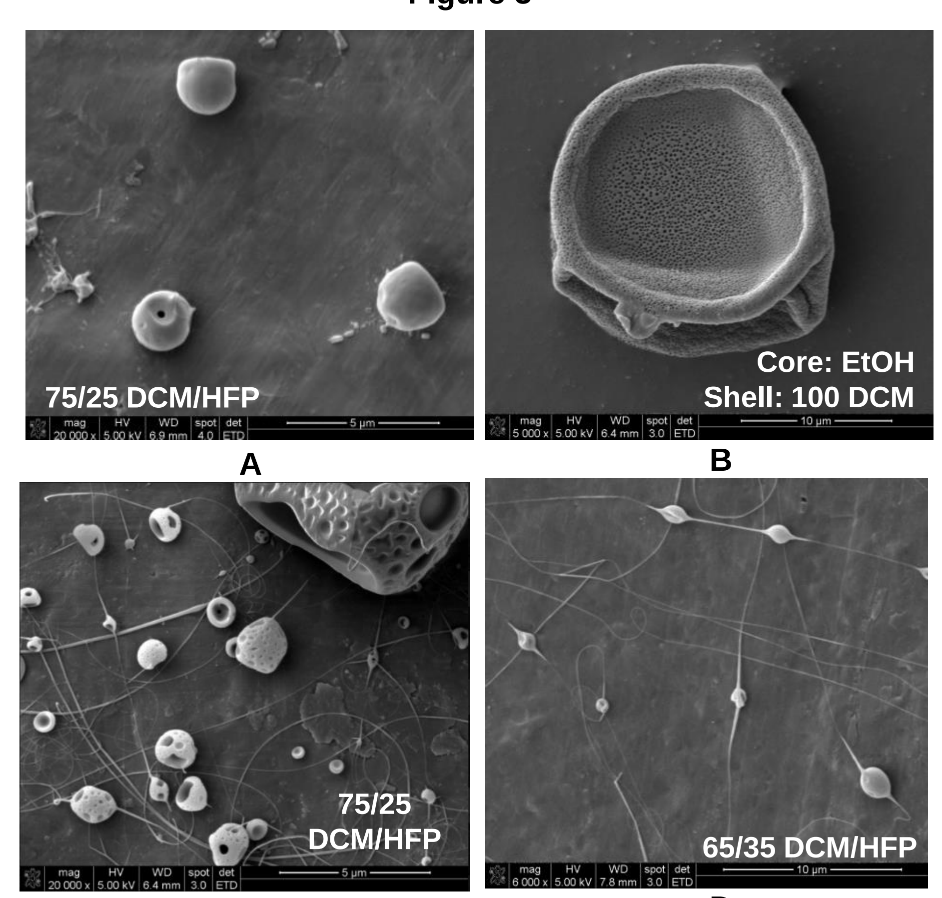


Figure 4: Graph depicting varied electrospraying distances and particle diameter relationship

__Figure 5A-D__: Core & Shell Solvent Ratio: X/Y DCM/HFP
__Figure 5B__: No Core Polymer (100% EtOH)
__Figure 5C__: Core Polymer: 3 wt% PSU

Figure 5



DISPERSION RESULTS

- Added dispersing agent to shell (Pluronic F-127)
- Developed solution sonication protocol : 5 mins on – 60 mins off – 5 mins on
- Plasma treated sample vials
- Analyzed using fluorescent microscopy

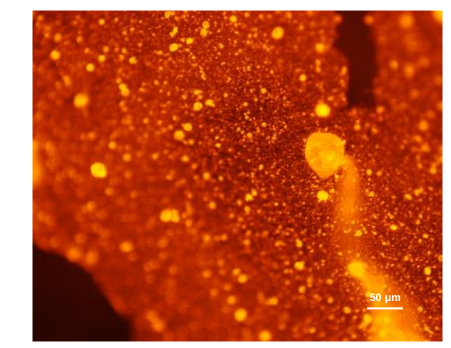


Figure 6: No Pluronic F-127

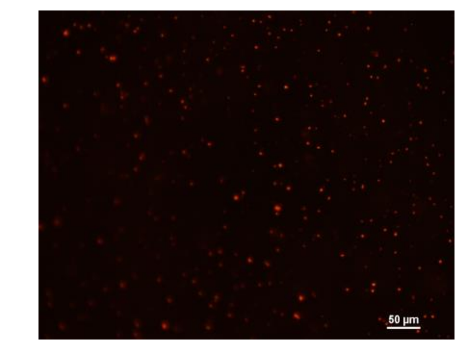


Figure 7: Pluronic F-127

LEACHING RESULTS

- 2 week Rose Bengal leaching test analyzed using a Fluorescence Microplate Reader at a temperature of ~37˚C

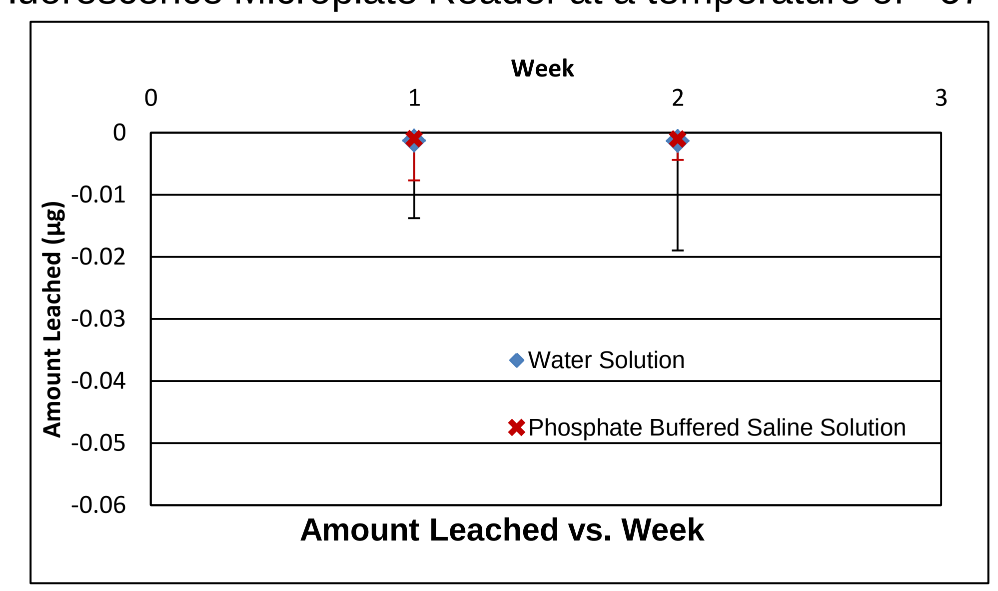


Figure 8: Amount of Rose Bengal leached over 2 weeks

CONCLUSION AND FUTURE WORK

- Solvent ratios and electrospraying distances have a strong affect on particle morphology.
- Current experiments have shown no leaching behavior.
- The dispersion agent in combination with the sonication process and plasma vials eliminate particle agglomeration.
- *Future work involves more detailed leaching tests and incorporating the UCNPs within the microparticles and testing the injectibility*

REFERENCES & ACKNOWLEDGMENTS

[1] Y. Amao, Probes and polymers for optical sensing of oxygen, Microchim. Acta. 143 (2003) 1–12. doi:10.1007/s00604-003-0037-x.
[2] Xue, Ruipeng, Prajna Behera, Mariano S. Viapiano, and John J. Lannutti. "Rapid Response Oxygen sensing Nanofibers." Materials Science and Engineering: C 33.6 (2013): 3450-457. Web.
[3] R.R. Anderson, J.A. Parrish, The optics of human skin., J. Invest. Dermatol. 77 (1981) 13–19.doi:10.1111/1523-1747.ep12479191.

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